

## Review article

# A systematic review on the trend of transcriptomic study in livestock: An effort to unwind the complexity of adaptation in a climate change environment

Putri Kusuma Astuti <sup>a,b,c</sup>, Péter Sárkány <sup>a</sup>, George Wanjala <sup>a,b,d</sup>, Zoltán Bagi <sup>a</sup>, Szilvia Kusza <sup>a,\*</sup>

<sup>a</sup> Centre for Agricultural Genomics and Biotechnology, University of Debrecen, Debrecen, 4032, Hungary

<sup>b</sup> Doctoral School of Animal Science, University of Debrecen, Debrecen, 4032, Hungary

<sup>c</sup> Department of Animal Breeding and Reproduction, Faculty of Animal Science, Universitas Gadjah Mada, Yogyakarta, 55281, Indonesia

<sup>d</sup> Institute of Animal Sciences and Wildlife Management, University of Szeged, Hódmezővásárhely, 6800, Hungary

## ARTICLE INFO

## Keywords:

Adaptation  
Climate change  
Heat stress  
Gene expression  
Livestock  
Transcriptomics

## ABSTRACT

Heat stress has been proven to cause negative effects on livestock leading to lower productivity and economic value. Understanding how heat stress manifests within an animal's body is the first step in devising a heat stress mitigation strategy; transcriptomic studies are one of the methods used. Here, using a systematic literature review methodology, we examine the recent decade of transcriptomics' application to the study of livestock adaptation. We identified 152 studies that met our criteria for using transcriptome methods to heat stress adaptation and were published within the last ten years. Our analysis demonstrates the growing popularity and application of transcriptome approaches in the investigation of the response of ruminants, pigs, and poultry livestock to heat stress. Majority of the works was done in chicken and cattle using multiple organs as the sample, with qRT-PCR as the most employed technique. It has been established that a variety of biomarkers can be used to assess animals under heat stress, such as the HSPs, ILs, and TLRs. Although transcriptomics has lately been employed extensively to uncover the mechanism of heat adaptation, this adaptive feature's complex mechanism remains unclear, leaving many knowledge gaps for investigation. A more complex studies involving more various cell types, organs, or even model organisms using multi-omics approach could be the future research direction in understanding the heat stress effects on livestock better.

## 1. Introduction

Recently, many “omics” technologies (genomics, metabolomics, transcriptomics, proteomics, etc.) have been brought to light in livestock research and have gained popularity in their application to the collecting of biological information; transcriptomics has emerged as one of the most significant in livestock animal. According to Lowe et al. [1] transcriptomics is used to investigate an organism's transcriptome, or the complete set of RNA transcripts produced. It provides information on gene structure, regulation of gene expression, gene product function, and genome dynamic in a specific tissue or cell type at specific developmental stage and/or

\* Corresponding author.

E-mail address: [kusza@agr.unideb.hu](mailto:kusza@agr.unideb.hu) (S. Kusza).

<https://doi.org/10.1016/j.heliyon.2024.e41090>

Received 8 August 2023; Received in revised form 4 December 2024; Accepted 9 December 2024

Available online 12 December 2024

2405-8440/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).

**Glossary**

RNA	Ribonucleic acid
DNA	Deoxyribonucleic acid
RNA-seq	RNA Sequencing
HSPs	Heat shock proteins
qRT-PCR	Quantitative real-time polymerase chain reaction
PBMCs	Peripheral blood mononuclear cells
ILs	Interleukins
TLRs	Toll-like receptors
NOS	Nitric oxide synthase
HSFs	Heat stress factors
HS	Heat stress
SLCs	Solute carrier family
GLUTs	Glucose transporters
FBP2	Fructose-bisphosphates 2
CATs	Catalase
SGLT1	Sodium/glucose cotransporter protein 1
SIRT1	Sirtuin 1
p-AMPK	AMP-activated protein kinase
CircRNA	Circular RNA
FSHB	Follicle stimulating hormone subunit beta
GH1	Growth hormone 1
PRL:	Prolactin
JAK/STAT	Janus kinase/signal transducers and activators of transcription
AP-1	Activator protein 1
NF- $\kappa$ B	Nuclear factor kappa B
CARNS1	Carnosine synthetase
SOD	Superoxide dismutase
MDA	Lipid peroxidation
MCRTs	Monocarboxylate transporters
PSE	Pale soft exudative
$\alpha$ RyR	$\alpha$ ryanodine receptor
CASQ1	Calsequestrin
AMPK $\alpha$ 2	AMP-activated protein kinase- $\alpha$ 2
M-CPT1	Carnitine palmitoyl transferase 1
avUCP	Avian uncoupling protein
FAS	Fatty-acid synthase
ACC	Acetyl-CoA carboxylase
PDK4	Pyruvate dehydrogenase kinase 4
CYPs	Cytochrome P450 family
MMPs	Matrix metalloproteinase
VTG2	Vitellogenin 2
COL2A1	Collagen type II alpha 1
KLF2	Kruppel-like factor 2
DNAJA4	DnaJ heat shock protein member A4
BAG3	Antiapoptotic BAG cochaperone 3
SERPINB2	Serpin family B member 2

under a specific physiological condition, which further shed light on the regulation network of biological process in a living organism [2].

Transcriptomics has made it possible to investigate how gene expression patterns differ under experimental and natural conditions, further understanding the biological process of adaptation [3]. Since gene expression links genotype to cellular and organismal physiology and, potentially, adaptive phenotypes, flexibility in gene expression can serve as a functional link in understanding the adaptation mechanism to the rapidly changing environments [4].

According to Rao et al. [5], transcriptome can basically be studied by two approaches: DNA microarray, a hybridization-based technique, and RNA-seq, a sequence-based approach. Research continues to find new applications for transcriptomics as a powerful, high-coverage, high-efficiency, and high-throughput analytical technique for obtaining genomic information on livestock. The mining of novel functional genes [6,7], the investigation of the synthesis pathways of secondary metabolites [8], the identification of

developmental pathways [9], and the acquisition of useful information for the breeding process [10] are just some of the areas where this method has already been put to use.

An example of a global recent research interest is the climate change, which is one of the most significant issues in the world and is anticipated to intensify; as evidenced by the fact that 2022 was recorded as one of the warmest years, 1.11° Celsius warmer than the 19th-century average [11], followed by extreme climate events such as heatwave, flood, wildfire, and droughts in some parts of the world [12]. In livestock farming, climate change is causing significant economic losses due to a decline in productivity in all aspects: reproduction, growth, meat and milk production (quantity and quality), and immunity [13–16]. The focus in the livestock farming industry has shifted from not only increasing productivity to including adaptation to climate change and animal welfare as key considerations. According to Abdu Niyas et al. [17], the term adaptation refers to the morphological, anatomical, physiological, and biochemical characteristics of an animal that, when combined, promote the animal’s welfare and favor its survival in a particular environment. In the context of the present work, adaptation refers to the animal’s ability to survive in the increasing global temperature or the heat stress (HS).

In order to have sustainable livestock production and protected biodiversity despite the current unexpected trend in environmental conditions, one of the most effective strategies would be to comprehend the cellular mechanism for responding to the changing environment.

Transcriptomic studies on specific topics in livestock science, such as male fertility [18], nutrigenomics [19], and prenatal nutrition [20], have been the subject of limited reviews. However, no recent reviews detail the expansion of transcriptomic applications in livestock adaptation and how these developments have occurred. In this review, we present the current state of transcriptomics applications in livestock science, with a focus on cattle, buffalo, sheep, goats, pig, and poultry adapting to the changing climate, highlighting the diversity of research locations, research goals, methods, and species. We noticed that there is a trend in transcriptomics study in livestock animals; majority of research has been done in cattle and chicken, with less work in any other livestock

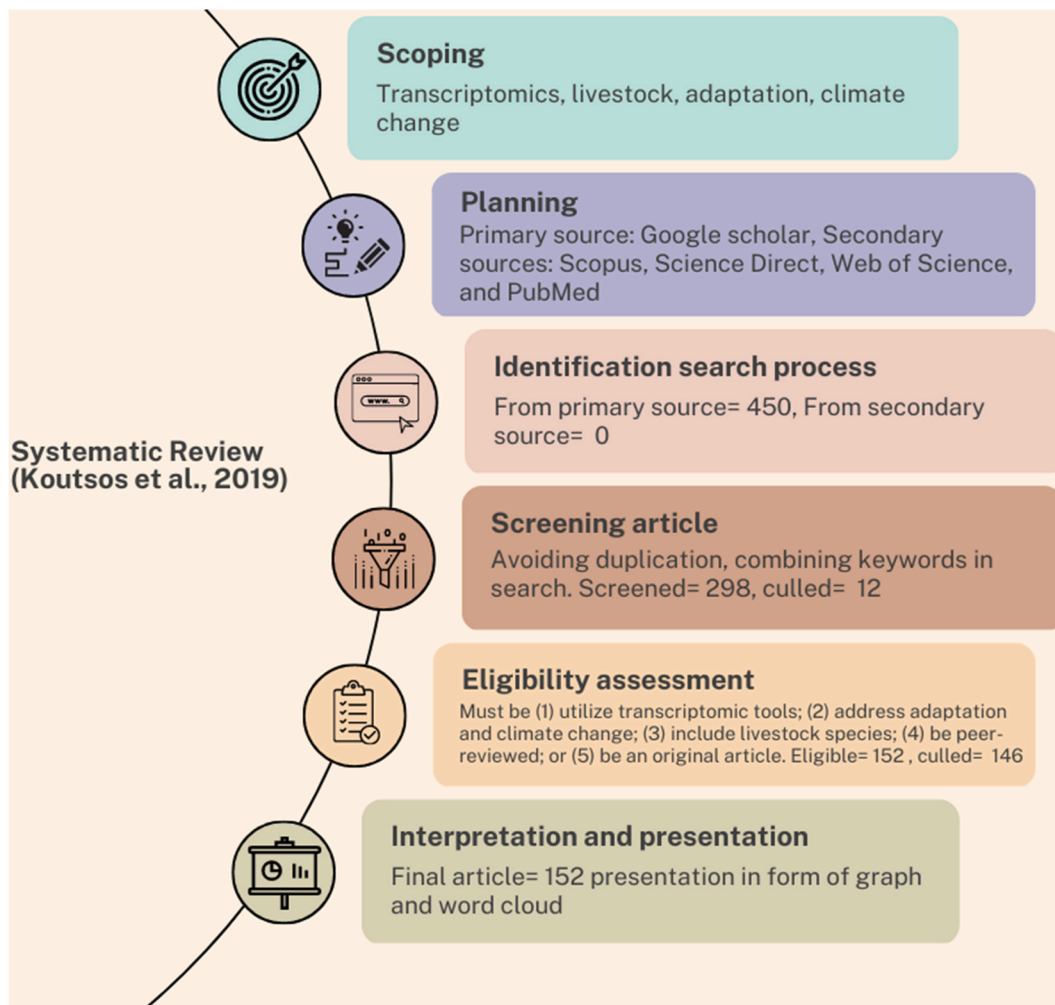


Fig. 1. A Flow chat of literature filtering criteria as applied in this study based on Koutsos et al. (2019).

species discussed in this review. Also, several genes highly related to heat stress adaptation has been found. Additionally, we highlight knowledge gaps and offer recommendations for the development of transcriptomics in the field of livestock science by expanding the research design by increasing the variety of samples organs, with combination of multiple omics technique, and also more complex comparison of species.

## 2. Material and method

This systematic review was conducted in accordance with the Koutsos et al. guidelines [21], which included six steps: (1) scoping, (2) planning, (3) identification search process, (4) screening article, (5) eligibility assessment, and (6) interpretation and presentation (Fig. 1). Accordingly, database of studies on the adaptation of livestock to climate change that employed transcriptomic techniques was compiled.

### 2.1. Database search

A preliminary comparison of multiple search engines with open access revealed that the majority of search results are comparable regardless of the search engine employed. In addition to Scopus (<https://www.scopus.com/>), the Web of Science (<https://www.webofscience.com/>), ScienceDirect (<http://www.sciencedirect.com/>), and PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>), Google Scholar (<https://scholar.google.com/>) was also selected as the primary literature search engine, as it yielded a substantial number of results, combining all major search engines, also not only limited to international and indexed journals. Adjustments were made to the configurations of all search engines and databases in order to increase the effectiveness of searches and filter out irrelevant results.

### 2.2. Search criteria

Only articles published between 2012 and 2022 containing keywords such as “transcriptome,” “gene expression,” “livestock,” “adaptation,” and “climate change” were considered due to the major development and application of transcriptomic studies in livestock animals. Consequently, each keyword combination generated a comprehensive list of results in the search engines.

### 2.3. Evaluation and screening process

They included various types of publications containing any or all keywords used. All retrieved publications were subjected to a manual review, and those that did not: (1) utilize transcriptomic tools to generate original data; (2) address adaptation and climate change; (3) include livestock species (cattle, buffalo, sheep, goats, pig, chicken, pigeon, quail, and duck); (4) be peer-reviewed; or (5) be an original article, were eliminated.

Majorly the challenges in this process were the duplicate articles and articles were not involving livestock species. We were focusing on the major livestock animals due to its economic significance and also its direct contribution in agricultural science to fulfil human needs in term of protein source. That is why, we were more focusing on the search result from Google Scholar, as its result were more comprehensive to detect all related articles.

### 2.4. Construction of database

After evaluating the obtained literature, the following information was entered into a database (Supplementary Table 1): (1) title, (2) DOI, (3) journal name, (4) volume, series, pages, (5) publication year, (6) keywords, (7) topics, (8) authors, (9) author origin, (10) corresponding authors email, (11) abstract, (12) species, (13) breeds, (14) sampling organs, (15) number of samples, (16) research environment; laboratory based or field based, (17) research conditions; natural condition or experimental treatment and (18) source of research funding.

### 2.5. Data analysis and result presentation

The database, which contained information manually assigned to each article, was utilized in subsequent analyses using R Software [22] and Excel [23], and visualizations utilizing Canva (<https://www.canva.com/>), San Diego, California, USA and RAWGraphs (<https://www.rawgraphs.io/>) [24].

## 3. Result

More than 10,000 results of scholarly articles published in between 2012 and 2022 were generated by the Google Scholar. Most of these articles were irrelevant to our study mainly due to the various object of research rather than livestock animals. We therefore used the keywords and specified for each type of livestock and retrieved 450 articles. All of the articles found in the secondary search engines were already accessible through the primary search engine, rendering the searches from the secondary search engines essentially ineffective.

After eliminating duplicates, irrelevant material, and ineligible studies, 152 articles from 2012 to 2022 are included for further analysis; this includes 61 ruminant-related papers, 26 pig-related papers, and 65 poultry-related papers. Most studies were eliminated

because their research designs, involved nutrition intervention to reduce heat stress rather than heat stress adaptation. The 152 publications came from 17 different countries; the largest numbers of articles were written by writers in India (n = 43), China (n = 31), the United States (n = 10), and a collaboration of many countries (n = 26) (Figs. 2 and 3).

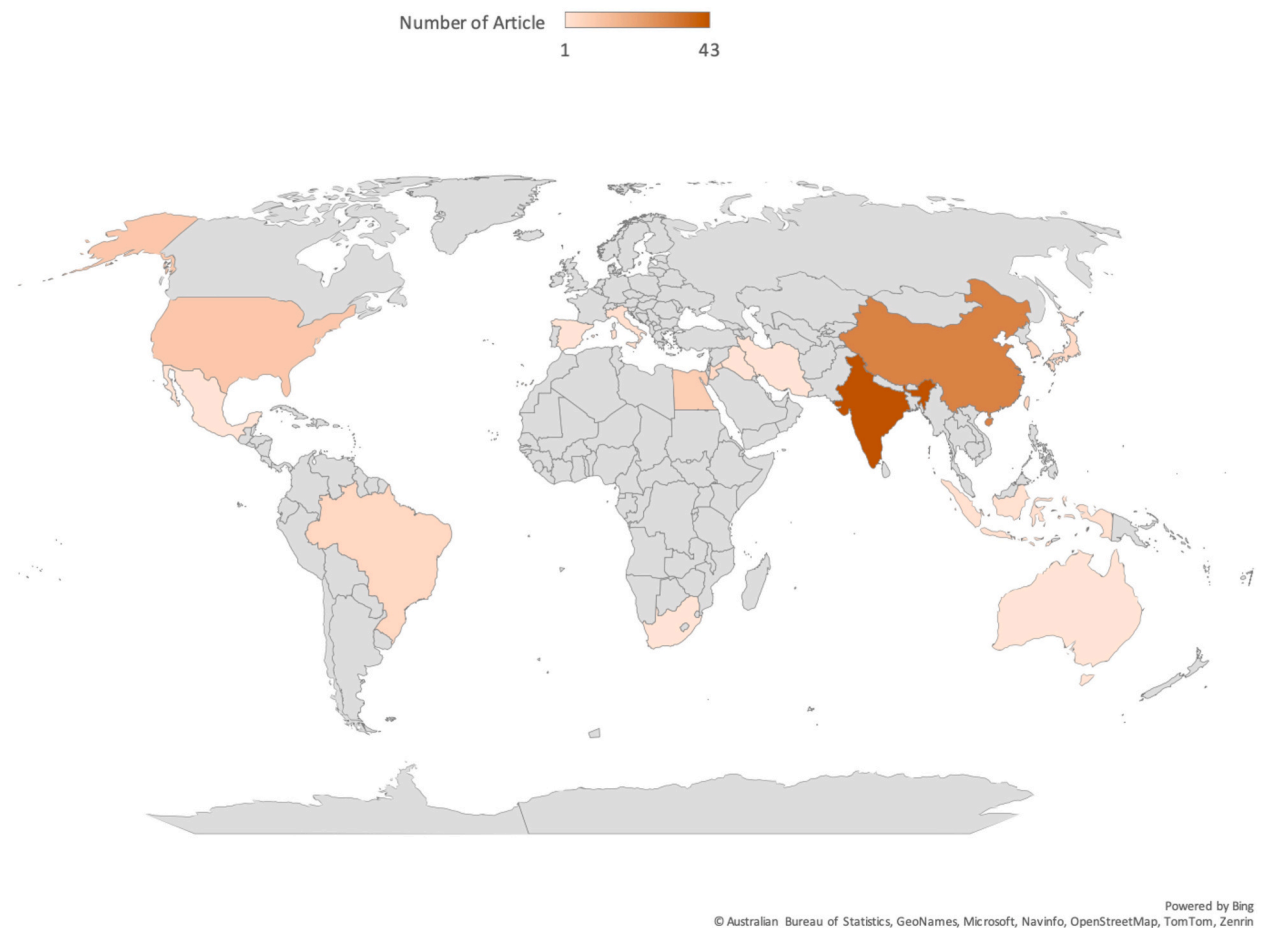
Most of the 346 keywords extracted from the 152 articles related to the heat adaptation. The most used keywords are heat stress (n = 81), heat shock proteins (HSP) (n = 25), and HSP70 (n = 20), gene expression (n = 17), broiler (n = 13), and pigs (n = 13) (Fig. 4).

A species-by-species breakdown for the ruminant and poultry categories was made. Cattle (n = 25), goat (n = 19), buffalo (n = 8), sheep (n = 4), cattle and buffalo (n = 4), and sheep and goat (n = 1) were all studied as part of the ruminant group (Fig. 5A). Chicken (n = 47), duck (n = 9), quail (n = 6), pigeon (n = 1), turkey (n = 1), and quail & turkey (n = 1) were the poultry species studied (Fig. 5B).

Fig. 6A shows that qRT-PCR was employed by the vast majority of the articles (n = 104), with blood as the sampling organ (n = 46) of and multiple organs (n = 40) being used out of the 152 studies (Fig. 6B). The sample sizes ranged from 5 to 250, with the big number of sample usually are blood sample and the highest number was involving oocyte sample. The majority of experimental observation settings (n = 119) were identified in laboratories (n = 86), indicating that the conditions setting in understanding heat adaptability have been constructed rather than in natural conditions (Fig. 6C and 6D).

#### 4. Discussion

Heat stress adaptation has recently emerged as a limiting factor in livestock farming due to its role in maintaining optimal livestock productivity and animal welfare in the face of climate change. Numerous investigations have been made using a variety of approaches and techniques to better understand the mechanism of temperature adaptation in animals. Transcriptomics is one approach that has gained popularity recently and has been used to investigate heat stress adaptation at the molecular level. Consequently, a deeper understanding of transcriptome regulation is offered. It has been successfully applied to address a wide range of concerns about the adaptability of organisms in a particular context, whether the natural state or through an experimental condition/induced treatment.



**Fig. 2.** Geographic heatmap based on the author origin of the 152 research articles from 2012 to 2022 related to transcriptomics study in livestock heat adaptation.

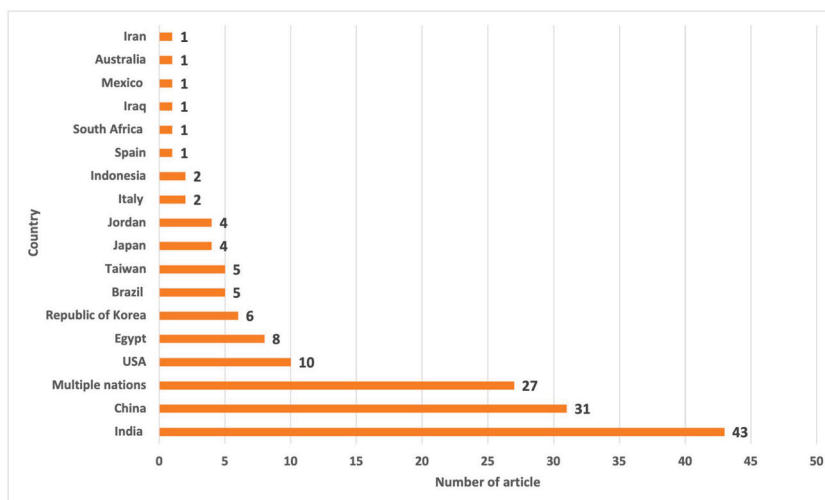


Fig. 3. Bar chart of the author origin of the 152 research article in 2012–2022 related to transcriptomics study in livestock heat adaptation.

Our collected literature shows that quantitative real-time- polymerase chain reaction (qRT-PCR) has been widely used in livestock studies. It is the most sensitive method for mRNA quantification due to its ability to detect uncommon transcripts and monitor minor changes in gene expression. It is a popular method for measuring transcript abundance because of its speed, throughput, and possibility for automation. When small quantities of sample are available, qRT-PCR is a great option since it allows for the simultaneous evaluation of gene expression in many separate samples for a restricted number of genes moreover, with well-defined data processing and workflows [25,26]. However, it is constrained by a slow processing rate, high per-cell costs, and extensive manual labor. Only up to four fluorescent dyes can be multiplexed, and separate assays and carefully tested primers are required for each gene. This implies that RT-qPCR is a hypothesis-driven technique that necessitates the selection of target genes based on prior knowledge, which may result in a biased analysis [27].

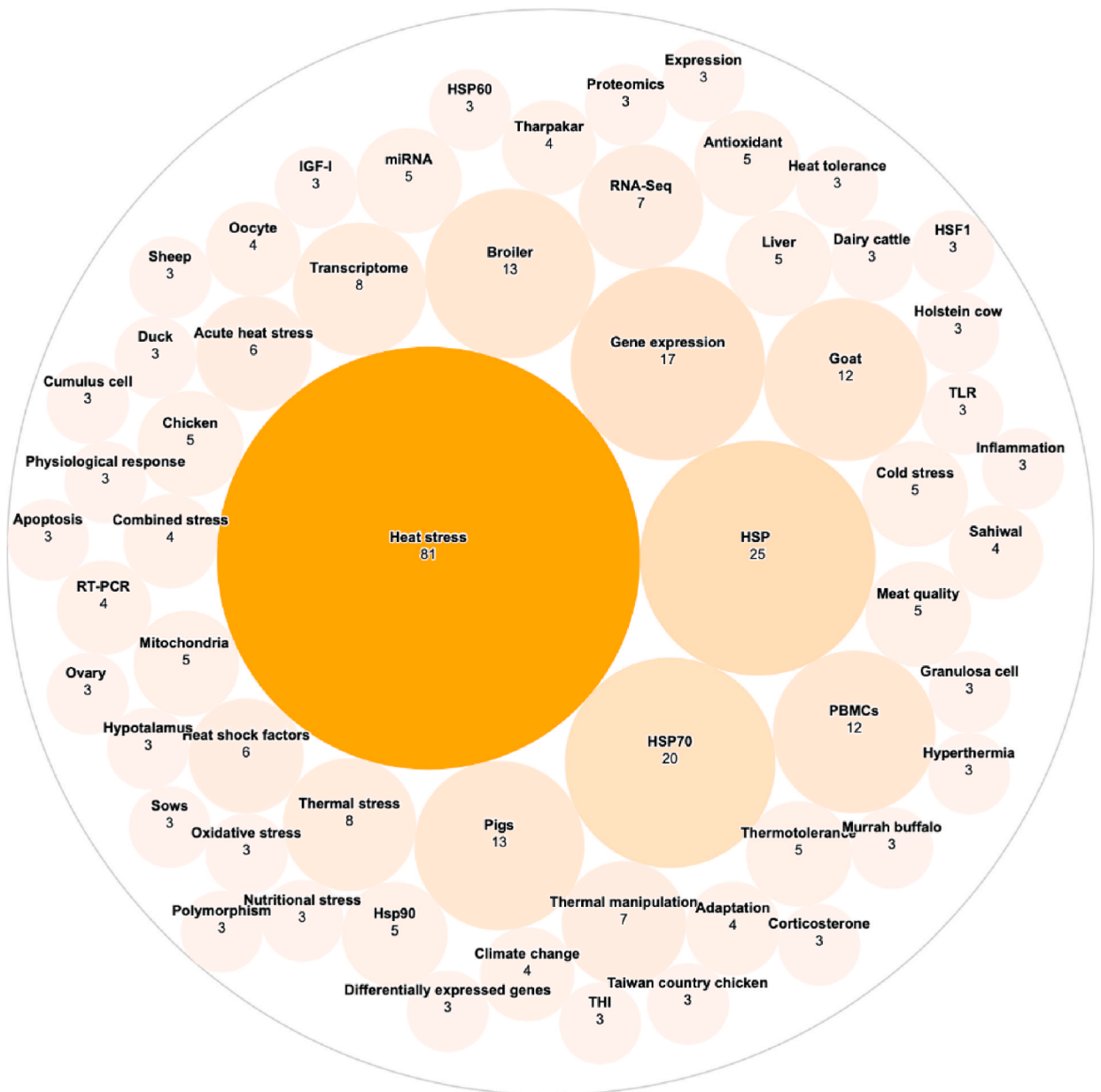
RNA-seq, on the other hand, has been widely considered the top approach for whole transcriptome gene expression quantification since its introduction in 2008 [28], with several advantages; no prior information of the transcriptome is necessary; it allows for a considerably more thorough examination of alternative splicing events; and it has a far greater dynamic range and is more sensitive than microarrays. Nonetheless, RNA-seq still confronts barriers in data processing and analysis, as well as cost, which, despite having decreased considerably in recent years, remains a barrier to even more widespread usage [29,30].

Rapid cellular adaptation was regulated transcriptionally in a short period of time to adapt to the changing environment. Evidence for the role of changes in transcriptome regulation in the adaptation process may be found in differentially expressed genes [31]. Several molecular mechanisms underlie the HS responses in animals, and these mechanisms can have direct effects on metabolite composition. As blood plays a crucial role in maintaining homeostasis, it remains the optimal choice for studying transcriptomic studies of thermal adaptation. According to Kishore et al. [32], the ability of peripheral blood mononuclear cells (PBMCs) to respond to HS in the laboratory makes them a useful biological model for studying the stress response in livestock. Moreover, PBMCs are a widely used cell model that can be easily extracted and cultivated to represent the overall animal's physiological state [33].

In thermal adaptation, various genes have been identified to play critical roles function as molecular chaperones, repress protein synthesis, and transport proteins during HS, such as Heat stress proteins (HSPs) [34,35], Interleukins (ILs) [36], Toll-like receptors (TLRs) [37,38], and many more. Many studies have focused on the HSPs, examining their regulation, cellular localization, and functions. HSPs are members of an extensive group of proteins that function as an integrated system to preserve proteostasis. Different stressors trigger the synthesis of HSPs, suggesting these "housekeeping" proteins play a crucial role in the physiology and biology of stressed cells. Increased HSP levels and expression of thermotolerant genes have been identified as the cell's ultimate response to HS, providing unquestionable evidence of its suitability as a biomarker; they act as chaperone to facilitate the folding, unfolding, and refolding of stress-denatured proteins. The HSP60/70/90 families are the most extensively researched among the various HSPs. In animal, HSP70 is one of the most studied genes, as it is a highly conserved, sensitive, and abundant gene that is associated with stress response. It is also has a strong correlation with thermotolerance in animals [33,39]. The trend in utilization of transcriptomics study in each livestock grouping (ruminant, pig, and poultry) is elaborated as follows.

#### 4.1. Ruminant

When it comes to adaptability, our attention will be focused mostly on indigenous breeds, whose adaptability has been demonstrated by their existence in that specific place. As one of the primary objectives is to determine which animals are best able to withstand the steadily increasing ambient temperature, a comparison of breeds assumes an important role, such as between the indigenous; Barki vs. Abu Dlik sheep [39], Sahiwal vs. Tharpakar cattle [40], Barbari vs. Jamunapari goat [41], Osmanadi vs. Salem

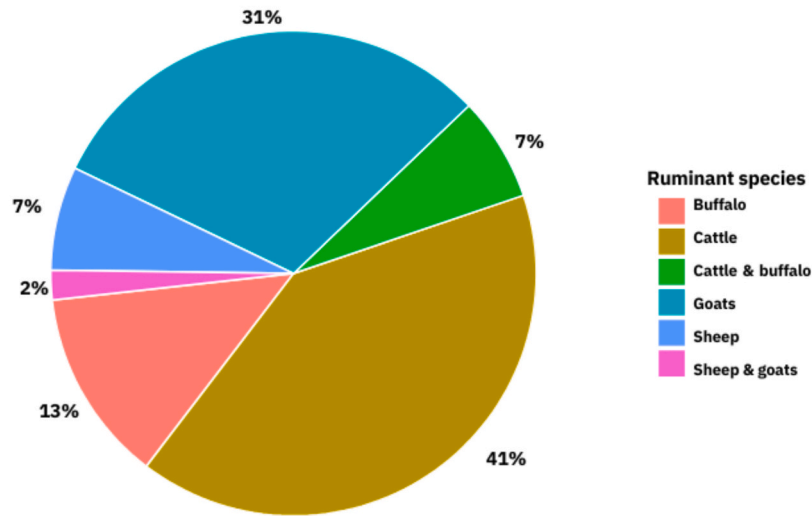


**Fig. 4.** Circle pack of the 58 most used keywords, which appeared more than 2 times within 152 publication articles in this study. The size of the circle and the intensity of the colour indicates the frequency with which they appear in the publication.

black goats [42], or between distinct breeds or crossbreds; Murrh buffaloes, Holstein–Friesian, and Sahiwal cows [32], Tharpakar and Karan Fries crossbred [43], Sahiwal and Holsten Friesian x Sahiwal crossbred [44]. Maibam et al. [43] and Kumar et al. [40] discovered that the expression pattern of specific HSPs genes varied depending on the livestock breed. These results could be due to morphological differences across breeds in thermotolerance and adaptability to different climatic circumstances, such as variances in coat color, skin thickness, and hair/wool length, which aid in the absorption and dissipation of heat [45], implying that when designing interventions to mitigate the effects of HS on animal health and productivity, breed and its origin are important factors to consider.

One of the well-known examples of the application of transcriptomics studies in natural settings is the seasonal dynamics of gene expression of HS-related genes, for example, HSPB9 and HSPB10 in testes of Hainan Black goats (2–2.5 years) under controlled environment under temperature about 18 °C, 25 °C, and 35 °C for 96 h [46] and nitric oxide synthase (NOS) and HSPs in female Barbari goats (4–5 years) under several peak season condition [47]. These studies aimed to understand how cellular regulation to the thermal stressor. Rawash et al. [48] discovered that summer heat (THI>80) negatively impacted the expression of IL2 and IL6 genes in

**A**



**B**

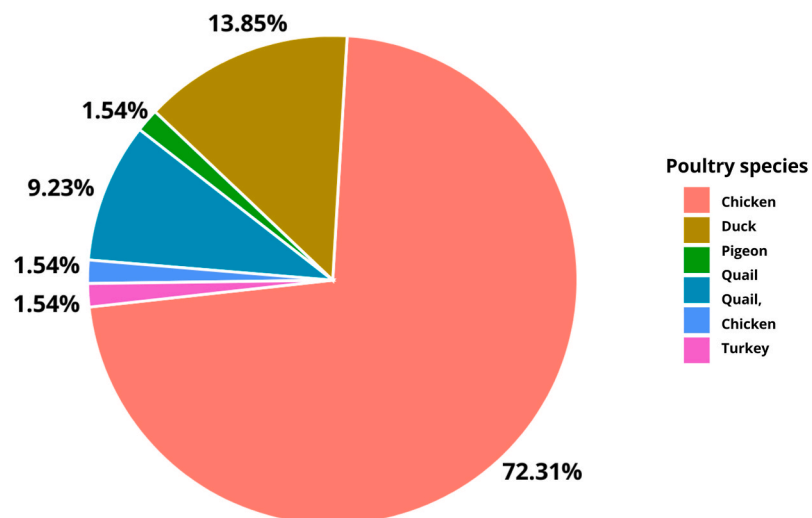
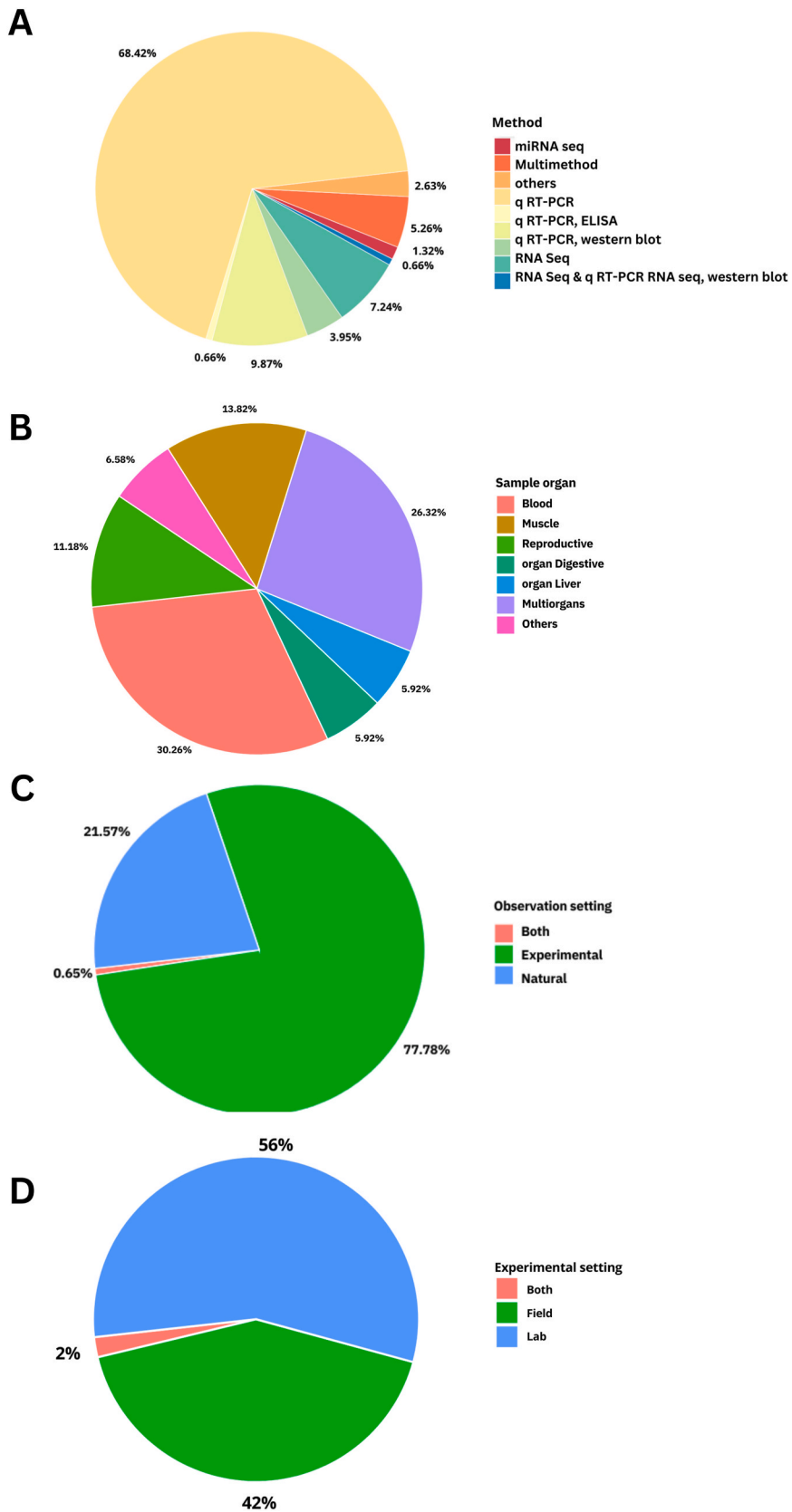


Fig. 5. Bar plot of number of articles of (A) ruminant species and (B) poultry species.

Barki ewes (3–4 years) while positively impacting the expression of HSP70 genes. Activating the immune response to reduce the negative consequences of chronic HS adaptation largely depends on the actions of these two immune-related genes. In addition to the Sahiwal and Kankrej cattle [49], the Barbari and Jamunapari goats [41], and the Murrah buffalo [40] all showed an upregulation of all the main HSPs during the warmer months of summer rather than other seasons.

HS is known to negatively impact livestock performance, especially reproduction. As a result, various research has been done to study the relationship between the two in ruminants. A study conducted on the Hainan black ram (2–2.5 years) by Xun et al. [46] revealed a high level of HSPB9 in the testes' convoluted seminiferous tubules' spermatogenic cells (spermatogonia, spermatocytes, and



(caption on next page)

**Fig. 6.** Bar plot of percentage of transcriptomic method employed collected article (A), the sampling organ (B), the observation setting; experimental set up, natural set up, or the combination of both (C), and the experimental setting in conducting the research; in the field, laboratory, or both (D).

spermatids). On the other hand, HSPB10 was predominantly expressed in elongated spermatids. The elevated levels of these two heat shock proteins at various stages of spermatogenesis suggest that they are essential for male reproduction and heat tolerance. HSPB9 may play a role in protecting and repairing spermatogenic cells from harm caused by HS, whereas HSPB10 may aid in the maturation and development of sperm cells. In female buffalo reproduction, high ambient temperature has been shown to have a deleterious impact on the maturation and subsequent embryo development processes at various cell stages. This was demonstrated by increased Heat stress factors (HSF)-1 and HSP90 mRNA expression in mature oocytes after HS, while HSF1, HSF2, HSP70, and HSP90 mRNA expression is considerably enhanced in cumulus cells. These findings imply that seasonal variations should be considered in buffalo breeding programs to mitigate the deleterious effects of HS on reproductive performance [50,51]. Taking this notion one step further, Yadav et al. [52] investigated the thermoneutral zone in buffalo by combining proteomics, physiological and biological responses to high temperatures, as a mitigation strategy for buffalo management under climate change scenarios.

#### 4.2. Pig

Morbidity, mortality (especially in market-weight hogs), suboptimal growth, inconsistent market weights, inefficient nutrient use, poor sow performance, reduced carcass value (increased lipid and decreased protein content), and carcass processing problems all increase when HS is present in pig farming [53].

In term of growth, HS has been demonstrated to be having a significant impact on pigs even at the very beginning of their lives. Sows exposed to high ambient temperature during neonatal period and early lactation, substantially increased the expression of HSP70 in the liver and abdominal fat of the piglets, as well as the expression of HSP27 in the liver. Both genes play a role in lipogenesis. During HS, glycogenesis was enhanced, providing scientific support for the observation of increased fatness and reduced muscle mass in thermally stressed pigs [54], which was also observed by Pearce et al. [53] in growing gilts under constant heat stress condition of 35 °C ± 1 °C; 20%–35% relative humidity for 7 days. Zhao et al. [55] observed that maternal HS under cyclic heat stress condition of 33 °C between 0900 h and 1700 h, and 28 °C between 1700 h and 0900 h for 3 weeks harms neonatal development by lowering the expression of genes associated with major nutrient transporters such as solute carrier family 7 member 8 (SLC7A8), solute carrier family 38 member 3 (SLC38A3), solute carrier family 15 member 1 (SLC15A1), glucose transporter 2 (GLUT2), and fructose-bisphosphates 2 (FBP2).

Pigs exposed to HS conditions have a 20% drop in feed intake and a doubled respiration rate, resulting in a 23% reduction in weight gain when compared to thermoneutral pigs. HSP90 expression in the duodenum and longissimus muscle was higher in HS pigs than in thermoneutral pigs, suggesting that HSP90 are significant components of their (pig's) long-term acclimatization mechanism. The presence of GLUT4 in the semitendinosus muscle and liver suggests an insulin-stimulated increase in glucose absorption by both tissues. The observed variations in Catalase 1 (CAT1), sodium/glucose cotransporter protein 1 (SGLT1), and GLUT4 expression suggest that heat stressed pigs make specialized modifications to preserve nutrient availability for the cells [56].

The HSP chaperone machinery in a pig's ovary is also constantly active and responsive to in vitro thermal exposure of 41.5 °C applied for 1 h, as stated by Pennarossa et al. [57]. Different members of the HSP40, HSP70, HSP90, HSP110, HSF1 and HSF2, were expressed in the ovarian follicles. Heat stress disturbed oocyte maturation and upregulated some HSP and HSF genes in entire pig ovaries, however the effects were only seen in oocytes and not cumulus cells. Seibert et al. [58] also reported this cell-specific response to HS in post pubertal gilts; they discovered that cyclic HS decreased HSP90AB1 and increased HSPB1, HSF1, and HSPD1 protein abundance in the ovary and corpus luteum during the follicular phase and luteal phase, respectively. In conclusion, the problem with lower fertility in sows during warm months was most likely caused by the inability of the surrounding cumulus cells and the entire follicle to respond effectively. This could be because the somatic and germinal compartments have different reaction levels.

Itami et al. [59], on the other hand, discovered a favourable effect of short term in vitro HS (41.5 °C for 1 h), which boosted mitochondrial degradation and biogenesis in pig oocytes, resulting in enhanced blastocyst development. HSP72, sirtuin 1 (SIRT1), and phosphorylation of AMP-activated protein kinase (p-AMPK) expression levels were likewise elevated after SHS treatment, indicating that HSP72 may be a causative activator of SIRT1 expression in oocytes, which improves mitochondrial quality in oocytes. According to the findings, short-term HS could be an effective non-invasive treatment for improving oocyte quality, which could be useful for assisted reproductive technologies.

In pig, the use of transcriptomic study in thermal stress adaptability was more focused on its impact on growth and meat quality. Main object of transcriptomic studies in pig is on skeletal muscle by utilizing various methods [60–64]. RNA-seq analysis revealed that chronic HS at 30 °C for 21 days caused differential expression of 78 genes in castrated pig *longissimus dorsi* muscle, linked to muscle form and function, glycolysis, lactate metabolism, lipid metabolism, cellular defense, and stress response. Variations in metabolic profiles and muscle composition resulted from chronic HS-induced transcriptome modifications, which led to poor meat quality [60]. In a novel approach, circular RNA (circRNA), a type of noncoding RNA, has been found to potentially act as a sponge for microRNA, sequestering and competitively suppressing their activity. They reported 59 circRNAs were found to be differentially expressed heat-stressed sow's pituitary gland under 37 °C and ~40% humidity, for 2–6 h, with 42 upregulated and 17 downregulated circRNAs, which play role in regulating specific pituitary genes and HS-related genes, including follicle stimulating hormone subunit beta (FSHB), growth hormone 1 (GH1), prolactin (PRL), HSP, and HSF, which are involved in hormone synthesis and stress response [65].

Long-term exposure to heat reduces IL6, which influences the janus kinase/signal transducers and activators of transcription (JAK/STAT) signalling, while short-term HS increases inflammatory signalling in pig skeletal muscle through the Activator protein 1 (AP-1) pathway and early Nuclear factor kappa B (NF- $\kappa$ B) pathway activation. HS leads to muscle dysfunction such as alteration of muscle physiology and increased muscle oxidative injury, which negatively impact on both animal welfare and meat production [63,64]. Also in term of meat quality, when longissimus dorsi muscle was exposed to 30 °C heat for three weeks, the mRNA expression of carnosine synthetase (CARNS1) was significantly lower than when the muscle was exposed to thermoneutral conditions. Heat exposure reduced antioxidant capacity (Superoxide dismutase (SOD) and Catalase (CAT)) and enhanced lipid peroxidation (MDA), indicating the presence of oxidative stress. As a result, the pork meat produced from heat-exposed muscle had lower pH, a\* values, and tenderness, as well as increased drip loss and L\* values as a result of changes in the expression of numerous proteins involved in muscle function and metabolism [66,67]. A study in crossbred pigs by Cui et al. [67] for three weeks showed that a total of 23 differentially expressed proteins were found between the control group at 22 °C artificial climate chamber and the HS group at 30 °C, these proteins are involved in carbohydrate metabolism, myofibrillar and cytoskeleton structure, stress response, antioxidant and detoxification, calcium binding, and cellular death.

Breed comparison was also done for pig for thermal adaptability. A study was done in Indian native, crossbred, and exotic pig by Vashi et al. [68]. Summertime (THI 80.92  $\pm$  0.5) HSP70 mRNA expression of PBMC was greater in almost all age groups (grower, finisher, sow, and boar) of crossbred and exotic pigs compared to other seasons. Parkunan et al. [69] discovered similar results for HSP70, HSP90, and monocarboxylate transporters (MCTs) in Chungroo and Large White Yorkshire pigs under summer heat stress of THI 82. According to two studies, similar to findings in ruminant studies, native pigs have innate mechanisms to regulate their body temperature in response to the high humidity and subtropical climate of their local environment, making them a reliable option in the face of rising global temperatures that may provide a more sustainable and resilient alternative to crossbred and exotic breeds for future livestock production.

### 4.3. Poultry

Multiple tissue comparisons are prevalent in poultry transcriptomic research, e.g. using liver, heart, muscle, brain, lung, and digestive organs tissue. Although their mechanism are still not fully elucidated, certain studies have established the tissue-specific distribution of HS-related genes [70–72], which corresponds to their unique functions in preventing tissue damage. For example, Xie et al. [73] reported that HSF1 and HSF4 were significantly less abundant than HSF2 and HSF3 in 31 weeks laying chicken muscle, and changes in the expression of HSF genes were not observable in muscle following thermal treatment (acute heat stress: up to 35 °C and chronic heat stress: cyclic 25-32-25 °C), despite significant variations in the heart and liver following acute heat stress. According to HSP70 and HSP90 expression, the heart is most responsive to heat challenges, while the muscle is least responsive, which may contribute to tissue injury by protein oxidation. In broiler chicken [74], higher expressions of HSP90 and HSP60 mRNA were detected in the muscle and heart compared to the brain, moreover after thermal manipulation of 39 °C for 18 h daily during embryonic days 12–18. Important insights into the role of HSP60 in cellular defence have been obtained from a study of HSP60's expression in several >2 years old pigeon tissues; specifically, the study revealed that the pigeon's brain, heart, and crop are particularly sensitive to heat stress treatment (38 °C for 2–8 h) [75].

Pale soft exudative (PSE) turkey meat could be a result of inadequate response to heat stress because of the late upregulation of significant genes responsible for calcium regulation, such as  $\alpha$  ryanodine receptor ( $\alpha$ RyR),  $\beta$  ryanodine receptor ( $\beta$ RyR), and calsequestrin (CASQ1). This altered calcium release in skeletal muscles could cause hypermetabolism, leading to increased temperature, rapid pH decline, and ultimately, protein denaturation and loss of protein function [76]. Addition by Lu et al. [77], who reported that heat stress treatment caused a disruption in the redox status and energy-substance metabolism of chickens, resulting in a reduction in antioxidant capacity and an increase in oxidative stress. This was concluded based on their examination of the mRNA expression dynamics of key genes involved in energy metabolism, including AMP-activated protein kinase- $\alpha$ 2 (AMPK $\alpha$ 2), carnitine palmitoyl transferase 1 (M-CPT1), avian uncoupling protein (avUCP), fatty-acid synthase (FAS), acetyl-CoA carboxylase (ACC), and pyruvate dehydrogenase kinase 4 (PDK4), at two time points (7 and 14 days) following exposure to a temperature of 32 °C.

Several candidate markers for reproductive efficacy under HS conditions have been identified in both male and female birds. In female, in addition to the HSPs genes, several other candidate genes have been confirmed, including cytochrome P450 family 11 subfamily A member 1 (CYP11A1), cytochrome P450 family 19 subfamily A member 1 (CYP19A1), CXC chemokines, and matrix metalloproteinase 3 (MMP3) in duck (Yang et al., 2021), and also IL6, vitellogenin 2 (VTG2), matrix metalloproteinase 13 (MMP13), collagen type II alpha 1 (COL2A1) and kruppel-like factor 2 (KLF2) in 30 weeks old broiler chicken under acute heat stress at 38 °C [78]. This reproductive disruption was through inhibition of proliferation, oestrogen synthesis, follicular growth, proteolytic disintegration, follicle cell damage, and many more. While in male birds, according to observation of acute heat-stressed (at 38 °C and 55 % relative humidity for 4 h with or without recovery) 45 weeks old roosters testes [79], HSP genes and co-chaperones (HSP70, HSP90AA1, HSP25, and DnaJ heat shock protein member A4 (DNAJA4)), antiapoptotic BAG cochaperone 3 (BAG3) and serpin family B member 2 (SERPINB2) were observed. These genes, particularly HSP25, may be crucial and unique critical components in the heat-stress response of avian testes.

Comparisons across strains are frequently undertaken in an attempt to identify markers that will facilitate the selection and breeding of more heat-tolerant poultry strains. The expression of the liver HSP70 gene in heat-stressed Ross broilers was significantly higher than in Cobb broilers kept under heat-stressed conditions for 4 or 6 h. This may be due to the significantly reduced antioxidant activity in heat-stressed Ross broilers, which corresponds to a lower serum SOD level [80]. Similar finding was as also mentioned by Zagloul et al. [81] according their observation in HSP90 genes expression, and Cedraz et al. [82] on observation of HSP70 between

local Brazilian strains (Caneluda and Peloco) and Cobb commercial strain, agreeing that Cobb strain is more vulnerable to heat stress. Incorporation of local indigenous strains' genetics in developing commercial strain was also suggested, due to their excellent thermal adaptability [83–85].

#### 4.4. Authors opinion on what approach can aids to understand cell's response to heat stress better

A number of studies on heat stress adaptation have been conducted using transcriptomics. However, the present study designs are often focused on just one aspect or particular objective only, for example, limited to several genes of interest or some organ samples only. We recognize that performing comprehensive research is not only challenging, but also expensive in terms of funds and labour, which not all researchers can afford. But, if a suggestion can be made, a combination of experimental techniques and advanced technologies is an opportunity to improve the understanding of a cell's response to heat stress from multiple observation points. Combination of multi-omics technology; genomics, transcriptomics, proteomics, and metabolomics, will also able to comprehensively study the changes occurring in cells during heat stress. By analysing thousands of genes, transcripts, proteins, and metabolites all at once at specific heat stressors amount or taking into account the gradual time of exposure, these methods provide a comprehensive view of cellular responses and enable the characterization of critical regulatory components at cellular level. The focus should not only to the stress related or immune related genes, but may also be expanded to production traits genes. Furthermore, as bioinformatics applications in livestock science develop, applying bioinformatics and computational modelling approaches to evaluate large-scale omics data and integrate information from diverse sources is becoming more common. This can help identify critical regulatory networks, pathways, and molecular interactions in the cellular response to heat stress.

Multiple sample research is currently available; however, bigger comparison studies involving higher coverage of genes, more various cell types, organs, or even comparison between model organisms to acquire insights into the general principles and conserved mechanisms of cellular response to heat stress are required. This can help identify important regulators and components involved by highlighting common pathways and molecular properties shared by diverse organisms; the closely related species to the most distinct ones.

## 5. Conclusion

This review outlines the trends in transcriptome studies regarding livestock adaptation to heat stress and emphasizes significant discoveries related to heat stress adaptation in ruminants, pigs, and poultry. Despite the increased accuracy of RNA-Seq, RT-qPCR remains the preferred method because of its ease of application and lower cost. Researchers continue to focus on heat shock proteins (HSPs) genes due to their key role in defending cells against heat stress, in addition to their roles in cell signalling, immunological response, and facilitating heat adaption. Toll-like receptors (TLRs), interleukins (ILs), and heat-shock transcription factors (HSFs) are a few more examples that have received attention in the past research works. In order to fully understand how cells respond to heat stress, multi-omics approaches that combine cutting-edge metabolomics and proteomics technologies will be important. Moreover, more extensive research with higher coverage of genes, more sample and species comparison might also be beneficial to acquire deeper knowledge in mechanisms of cellular response to heat stress. This review does not elaborate in detail on the livestock molecular adaptation to heat stress; however, it provides the audience with significant research trends that can serve as a reference for designing future studies aimed at enhancing the understanding of heat stress adaptation in livestock, because heat stress will remain essential to the cause of sustainable livestock farming in the midst of a constantly changing climate.

### CRedit authorship contribution statement

**Putri Kusuma Astuti:** Writing – original draft, Methodology, Data curation, Conceptualization. **Péter Sárkány:** Writing – review & editing, Data curation. **George Wanjala:** Writing – review & editing. **Zoltán Bagi:** Writing – review & editing. **Szilvia Kusza:** Writing – review & editing, Validation, Supervision, Conceptualization.

### Ethics declarations

Review and/or approval by an ethics committee was not needed for this review study.

### Data availability

All data used in this review is available in the supplementary materials.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgement

P.K.A. and G.W. were supported by Tempus Public Foundation within the Stipendium Hungaricum Programme. Supported by the University of Debrecen Program for Scientific Publication.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e41090>.

## Supplementary material

Excel database of the articles included in this study can be downloaded together with this article.

## References

- [1] R. Lowe, N. Shirley, M. Bleackley, S. Dolan, T. Shafee, Transcriptomics technologies, *PLoS Comput. Biol.* 13 (5) (2017) e1005457, <https://doi.org/10.1371/journal.pcbi.1005457>.
- [2] Z.C. Dong, Y. Chen, Transcriptomics: advances and approaches, *Sci. China Life Sci.* 56 (2013) 960–967, <https://doi.org/10.1007/s11427-013-4557-2>.
- [3] H.E. Rivera, H.E. Aichelman, J.E. Fifer, N.G. Kriefall, D.M. Wuitchik, S.J. Smith, S.W. Davies, A framework for understanding gene expression plasticity and its influence on stress tolerance, *Mol. Ecol.* 30 (6) (2021) 1381–1397, <https://doi.org/10.1111/mec.15820>.
- [4] E.B. Josephs, Gene expression links genotype and phenotype during rapid adaptation, *Mol. Ecol.* 30 (1) (2021) 30–32, <https://doi.org/10.1111/mec.15729>.
- [5] M.S. Rao, T.R. van Vleet, R. Ciurlionis, W.R. Buck, S.W. Mittelstadt, E.A.G. Blomme, M.J. Liguori, Comparison of RNA-seq and microarray gene expression platforms for the toxicogenomic evaluation of liver from short-term rat toxicity studies, *Front. Genet.* 9 (2019), <https://doi.org/10.3389/fgene.2018.00636>.
- [6] H. Peng, M. Hu, Z. Liu, W. Lai, L. Shi, Z. Zhao, H. Ma, Y. Li, S. Yan, Transcriptome analysis of the liver and muscle tissues of Dorper and small-tailed han sheep, *Front. Genet.* 13 (2022), <https://doi.org/10.3389/fgene.2022.868717>.
- [7] M.A. Scott, A.R. Woolums, C.E. Swiderski, A.D. Perkins, B. Nanduri, D.R. Smith, B.B. Karisch, W.B. Epperson, J.R. Blanton, Whole blood transcriptomic analysis of beef cattle at arrival identifies potential predictive molecules and mechanisms that indicate animals that naturally resist bovine respiratory disease, *PLoS One* 15 (1) (2020) e0227507, <https://doi.org/10.1371/journal.pone.0227507>.
- [8] L. Cao, X. Jin, Y. Zhang, M. Zhang, Y. Wang, Transcriptomic and metabolomic profiling of melatonin treated soybean (*Glycine max* L.) under drought stress during grain filling period through regulation of secondary metabolite biosynthesis pathways, *PLoS One* 15 (10) (2020) e0239701, <https://doi.org/10.1371/journal.pone.0239701>.
- [9] H.-Z. Sun, V. Srithayakumar, J. Jimenez, W. Jin, A. Hosseini, M. Raszek, K. Orsel, L.L. Guan, G. Plastow, Longitudinal blood transcriptomic analysis to identify molecular regulatory patterns of bovine respiratory disease in beef cattle, *Genomics* 112 (6) (2020) 3968–3977, <https://doi.org/10.1016/j.ygeno.2020.07.014>.
- [10] X. Meng, Z. Gao, Y. Liang, C. Zhang, Z. Chen, Y. Mao, B. Huang, K. Kui, Z. Yang, Longissimus dorsi muscle transcriptomic analysis of simmental and Chinese native cattle differing in meat quality, *Front. Vet. Sci.* 7 (2020), <https://doi.org/10.3389/fvets.2020.601064>.
- [11] NASA, NASA says 2022 fifth warmest year on record, warming trend continues, Retrieved January 26, 2023 from, <https://www.nasa.gov/press-release/nasa-says-2022-fifth-warmest-year-on-record-warming-trend-continues>, 2022.
- [12] M. Romanello, C. di Napoli, P. Drummond, C. Green, H. Kennard, P. Lampard, D. Scamman, N. Arnell, S. Ayeb-Karlsson, L.B. Ford, K. Belesova, K. Bowen, W. Cai, M. Callaghan, D. Campbell-Lendrum, J. Chambers, K.R. van Daalen, C. Dalin, N. Dasandi, A. Costello, The 2022 report of the Lancet Countdown on health and climate change: health at the mercy of fossil fuels, *Lancet* 400 (10363) (2022) 1619–1654, [https://doi.org/10.1016/S0140-6736\(22\)01540-9](https://doi.org/10.1016/S0140-6736(22)01540-9).
- [13] P.K. Astuti, G. Wanjala, Z. Bagi, S. Kusza, Coping with climate change; is white sheep more favorable than black? A review, *Allattenyész. Takarmanyozas* 71 (4) (2022) 270–281.
- [14] X. Chen, J.N. Dong, J.Y. Rong, J. Xiao, W. Zhao, N.D. Aschalew, X.F. Zhang, T. Wang, G.X. Qin, Z. Sun, Y.G. Zhen, Impact of heat stress on milk yield, antioxidative levels, and serum metabolites in primiparous and multiparous Holstein cows, *Trop. Anim. Health Prod.* 54 (3) (2022) 159, <https://doi.org/10.1007/s11250-022-03159-x>.
- [15] P.V. Spandan, W. Ruban, V. Sejian, C. Devaraj, M.V. Silpa, V.B. Awachat, G.B. Manjunathareddy, R. Bhatta, Heat stress induced changes in the major carcass traits and quantitative expression patterns of selective meat quality determining genes in Kanni Aadu Goats, *Food Chem. Adv.* 1 (2022) 100053, <https://doi.org/10.1016/j.focha.2022.100053>.
- [16] G. Wanjala, P.K. Astuti, Z. Bagi, N. Kichamu, P. Strausz, S. Kusza, A review on the potential effects of environmental and economic factors on sheep genetic diversity: consequences of climate change, *Saudi J. Biol. Sci.* 30 (1) (2023) 103505, <https://doi.org/10.1016/j.sjbs.2022.103505>.
- [17] P.A. Abdul Niyas, K. Chaidanya, S. Shaji, V. Sejian, R. Bhatta, M. Bagath, G.S.L.H.V.P. Rao, V. Girish, Adaptation of livestock to environmental challenges, *J. Vet. Sci. Med. Diagn* 4 (3) (2015), <https://doi.org/10.4172/2325-9590.1000162>.
- [18] R. Indriastuti, B.P. Pardede, A. Gunawan, M.F. Ulum, R.I. Arifiantini, B. Purwantara, Sperm transcriptome analysis accurately reveals male fertility potential in livestock, *Animals* 12 (21) (2022) 2955, <https://doi.org/10.3390/ani12212955>.
- [19] Z. ul Haq, A. Saleem, A.A. Khan, M.A. Dar, A.M. Ganaie, Y.A. Beigh, H. Hamadani, S.M. Ahmad, Nutrigenomics in livestock sector and its human-animal interface-a review, *Vet. Anim. Sci.* 17 (2022) 100262, <https://doi.org/10.1016/j.vas.2022.100262>.
- [20] A. Foroutan, D.S. Wishart, C. Fitzsimmons, Exploring biological impacts of prenatal nutrition and selection for residual feed intake on beef cattle using omics technologies: a review, *Front. Genet.* 12 (2021), <https://doi.org/10.3389/fgene.2021.720268>.
- [21] T.M. Koutsos, G.C. Menexes, C.A. Dordas, An efficient framework for conducting systematic literature reviews in agricultural sciences, *Sci. Total Environ.* 682 (2019) 106–117, <https://doi.org/10.1016/j.scitotenv.2019.04.354>.
- [22] R Core Team, R: A Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria, 2020. <https://www.R-project.org/>.
- [23] Microsoft Corporation, Microsoft Excel, Retrieved from, <https://office.microsoft.com/excel>, 2018.
- [24] M. Mauri, T. Elli, G. Caviglia, G. Uboldi, M. Azzi, RAWGraphs: a visualisation platform to create open outputs, in: Proceedings of the 12th Biannual Conference on Italian SIGCHI Chapter, 2017, pp. 28:1–28:5, <https://doi.org/10.1145/3125571.3125585>. New York, NY, USA: ACM.
- [25] C.R. Galiveti, T.S. Rozhdestvensky, J. Brosius, H. Lehrach, Z. Konthur, Application of housekeeping npcRNAs for quantitative expression analysis of human transcriptome by real-time PCR, *RNA* 16 (2) (2010) 450–461, <https://doi.org/10.1261/rna.1755810>.
- [26] A. Ho-Pun-Cheung, C. Bascoul-Molleivi, E. Assenat, F. Boissière-Michot, F. Bibeau, D. Cellier, M. Ychou, E. Lopez-Crapez, Reverse transcription-quantitative polymerase chain reaction: description of a RIN-based algorithm for accurate data normalization, *BMC Mol. Biol.* 10 (1) (2009) 31, <https://doi.org/10.1186/1471-2199-10-31>.
- [27] P. Angerer, L. Simon, S. Tritschler, F.A. Wolf, D. Fischer, F.J. Theis, Single cells make big data: new challenges and opportunities in transcriptomics, *Curr. Opin. Struct. Biol.* 4 (2017) 85–91, <https://doi.org/10.1016/j.coisb.2017.07.004>.

- [28] S.M. Jazayeri, L.M. Melgarejo-Muñoz, H.M. Romero, RNA-SEQ: a glance at technologies and methodologies, *Acta Biol. Colomb.* 20 (2) (2014), <https://doi.org/10.15446/abc.v20n2.43639>.
- [29] Z. Hou, P. Jiang, S.A. Swanson, A.L. Elwell, B.K.S. Nguyen, J.M. Bolin, R. Stewart, J.A. Thomson, A cost-effective RNA sequencing protocol for large-scale gene expression studies, *Sci. Rep.* 5 (1) (2015) 9570, <https://doi.org/10.1038/srep09570>.
- [30] C. Everaert, M. Luybaert, J.L.v. Maag, Q.X. Cheng, M.E. Dinger, J. Hellemans, P. Mestdagh, Benchmarking of RNA-sequencing analysis workflows using whole-transcriptome RT-qPCR expression data, *Sci. Rep.* 7 (1) (2017) 1559, <https://doi.org/10.1038/s41598-017-01617-3>.
- [31] H. Liu, X. Wang, M.L. Warburton, W. Wen, M. Jin, M. Deng, J. Liu, H. Tong, Q. Pan, X. Yang, J. Yan, Genomic, transcriptomic, and phenomic variation reveals the complex adaptation of modern maize breeding, *Mol. Plant* 8 (6) (2015) 871–884, <https://doi.org/10.1016/j.molp.2015.01.016>.
- [32] A. Kishore, M. Sodhi, P. Kumari, A.K. Mohanty, D.K. Sadana, N. Kapila, K. Khate, U. Shandilya, R.S. Kataria, M. Mukesh, Peripheral blood mononuclear cells: a potential cellular system to understand differential heat shock response across native cattle (*Bos indicus*), exotic cattle (*Bos taurus*), and riverine buffaloes (*Bubalus bubalis*) of India, *Cell Stress Chaperones* 19 (5) (2014) 613–621, <https://doi.org/10.1007/s12192-013-0486-z>.
- [33] H. Fang, L. Kang, Z. Abbas, L. Hu, Y. Chen, X. Tan, Y. Wang, Q. Xu, Identification of key genes and pathways associated with thermal stress in peripheral blood mononuclear cells of Holstein dairy cattle, *Front. Genet.* 12 (2021), <https://doi.org/10.3389/fgene.2021.662080>.
- [34] C.-Y. Cheng, W.-L. Tu, C.-J. Chen, H.-L. Chan, C.-F. Chen, H.-H. Chen, P.-C. Tang, Y.-P. Lee, S.-E. Chen, S.-Y. Huang, Functional genomics study of acute heat stress response in the small yellow follicles of layer-type chickens, *Sci. Rep.* 8 (1) (2018) 1320, <https://doi.org/10.1038/s41598-017-18335-5>.
- [35] S.I.U. Umar, D. Konwar, A. Khan, M.A. Bhat, F. Javid, R. Jeelani, B. Nabi, A.A. Najjar, D. Kumar, B. Brahma, Delineation of temperature-humidity index (THI) as indicator of heat stress in riverine buffaloes (*Bubalus bubalis*) of a sub-tropical Indian region, *Cell Stress Chaperones* 26 (4) (2021) 657–669, <https://doi.org/10.1007/s12192-021-01209-1>.
- [36] Y. Tsugami, Y. Ishiba, N. Suzuki, T. Nii, K. Kobayashi, N. Isobe, Local heat treatment of goat udders influences innate immune functions in mammary glands, *J. Mammary Gland Biol* 26 (4) (2021) 387–397, <https://doi.org/10.1007/s10911-022-09509-7>.
- [37] X.-H. Ju, H.-J. Xu, Y.-H. Yong, L.-L. An, P.-R. Jiao, M. Liao, Heat stress upregulation of Toll-like receptors 2/4 and acute inflammatory cytokines in peripheral blood mononuclear cell (PBMC) of Bama miniature pigs: an in vivo and in vitro study, *Animal* 8 (9) (2014) 1462–1468, <https://doi.org/10.1017/S1751731114001268>.
- [38] J. Bharati, S.S. Dangi, S.R. Mishra, V.S. Chouhan, V. Verma, O. Shankar, M.K. Bharti, A. Paul, D.K. Mahato, G. Rajesh, G. Singh, V.P. Maurya, S. Bag, P. Kumar, M. Sarkar, Expression analysis of Toll like receptors and interleukins in Tharparkar cattle during acclimation to heat stress exposure, *J. Therm. Biol.* 65 (2017) 48–56, <https://doi.org/10.1016/j.jtherbio.2017.02.002>.
- [39] F. Younis, Expression pattern of heat shock protein genes in sheep, *Mansoura Vet. Med. J.* 21 (1) (2020) 1–5, <https://doi.org/10.35943/mvmj.2020.21.001>.
- [40] A. Kumar, S. Ashraf, T.S. Goud, A. Grewal, S.V. Singh, B.R. Yadav, R.C. Upadhyay, Expression profiling of major heat shock protein genes during different seasons in cattle (*Bos indicus*) and buffalo (*Bubalus bubalis*) under tropical climatic condition, *J. Therm. Biol.* 51 (2015) 55–64, <https://doi.org/10.1016/j.jtherbio.2015.03.006>.
- [41] R. Nagayach, U.D. Gupta, A. Prakash, Expression profiling of hsp70 gene during different seasons in goats (*Capra hircus*) under sub-tropical humid climatic conditions, *Small Rumin. Res.* 147 (2017) 41–47, <https://doi.org/10.1016/j.smallrumres.2016.11.016>.
- [42] P.R. Archana, V. Sejian, W. Ruban, M. Bagath, G. Krishnan, J. Aleena, G.B. Manjunathreddy, V. Beena, R. Bhatta, Comparative assessment of heat stress induced changes in carcass traits, plasma leptin profile and skeletal muscle myostatin and HSP70 gene expression patterns between indigenous Osmanabadi and Salem Black goat breeds, *Meat Sci.* 141 (2018) 66–80, <https://doi.org/10.1016/j.meatsci.2018.03.015>.
- [43] U. Maibam, O.K. Hooda, P.S. Sharma, A.K. Mohanty, S.V. Singh, R.C. Upadhyay, Expression of HSP70 genes in skin of zebu (Tharparkar) and crossbred (Karan Fries) cattle during different seasons under tropical climatic conditions, *J. Therm. Biol.* 63 (2017) 58–64, <https://doi.org/10.1016/j.jtherbio.2016.11.007>.
- [44] J.K. Gill, J.S. Arora, B.V. Sunil Kumar, C.S. Mukhopadhyay, S. Kaur, N. Kashyap, Cellular thermotolerance is independent of HSF 1 expression in zebu and crossbred non-lactating cattle, *Int. J. Biometeorol.* 61 (9) (2017) 1687–1693, <https://doi.org/10.1007/s00484-017-1350-0>.
- [45] C.L.F. Katiyatiya, G. Bradley, V. Muchenje, Thermotolerance, health profile and cellular expression of HSP90AB1 in Nguni and Boran cows raised on natural pastures under tropical conditions, *J. Therm. Biol.* 69 (2017) 85–94, <https://doi.org/10.1016/j.jtherbio.2017.06.009>.
- [46] W. Xun, L. Shi, T. Cao, C. Zhao, P. Yu, D. Wang, G. Hou, H. Zhou, Dual functions in response to heat stress and spermatogenesis: characterization of expression profile of small heat shock proteins 9 and 10 in goat testis, *BioMed Res. Int.* 2015 (2015) 1–8, <https://doi.org/10.1155/2015/686239>.
- [47] V.P. Yadav, S.S. Dangi, V.S. Chouhan, M. Gupta, S.K. Dangi, G. Singh, V.P. Maurya, P. Kumar, M. Sarkar, Expression analysis of NOS family and HSP genes during thermal stress in goat (*Capra hircus*), *Int. J. Biometeorol.* 60 (3) (2015) 381–389, <https://doi.org/10.1007/s00484-015-1035-5>.
- [48] R.A.A. Rawash, M.A. Sharaby, G.E.-D.A. Hassan, A.E. Elkomy, E.E. Hafez, S.H.A. Hafsa, M.M.I. Salem, Expression profiling of HSP 70 and interleukins 2, 6 and 12 genes of Barki sheep during summer and winter seasons in two different locations, *Int. J. Biometeorol.* 66 (10) (2022) 2047–2053, <https://doi.org/10.1007/s00484-022-02339-6>.
- [49] G. Gujar, V.K. Choudhary, P. Vivek, M. Sodhi, M. Choudhary, M. Tiwari, N. Masharing, M. Mukesh, Characterization of thermo-physiological, hematological, and molecular changes in response to seasonal variations in two tropically adapted native cattle breeds of *Bos indicus* lineage in hot arid ambience of Thar Desert, *Int. J. Biometeorol.* 66 (8) (2022) 1515–1529, <https://doi.org/10.1007/s00484-022-02293-3>.
- [50] A. El-Sayed, R. Nagy, A.K. El-Asheeri, L.N. Eid, Developmental and molecular responses of buffalo (*Bubalus bubalis*) cumulus-oocyte complex matured *in vitro* under heat shock conditions, *Zygote* 26 (2) (2018) 177–190, <https://doi.org/10.1017/S0967199418000072>.
- [51] M.S. Faheem, N. Ghanem, A. Gad, R. Procházka, S.M. Dessouki, Adaptive and biological responses of Buffalo granulosa cells exposed to heat stress under *in vitro* condition, *Animals* 11 (3) (2021) 794, <https://doi.org/10.3390/ani11030794>.
- [52] P. Yadav, B. Yadav, D. Swain, M. Anand, S. Yadav, A. Madan, Differential expression of miRNAs and related mRNAs during heat stress in buffalo heifers, *J. Therm. Biol.* 97 (2021) 102904, <https://doi.org/10.1016/j.jtherbio.2021.102904>.
- [53] S.C. Pearce, N.K. Gabler, J.W. Ross, J. Escobar, J.F. Patience, R.P. Rhoads, L.H. Baumgard, The effects of heat stress and plane of nutrition on metabolism in growing pigs1, *J. Anim. Sci.* 91 (5) (2013) 2108–2118, <https://doi.org/10.2527/jas.2012-5738>.
- [54] J. Heng, M. Tian, W. Zhang, F. Chen, W. Guan, S. Zhang, Maternal heat stress regulates the early fat deposition partly through modification of m6A RNA methylation in neonatal piglets, *Cell Stress Chaperones* 24 (3) (2019) 635–645, <https://doi.org/10.1007/s12192-019-01002-1>.
- [55] W. Zhao, F. Liu, C.D. Marth, M.P. Green, H.H. Le, B.J. Leury, A.W. Bell, F.R. Dunshen, J.J. Cottrell, Maternal heat stress alters expression of genes associated with nutrient transport activity and metabolism in female placentae from mid-gestating pigs, *Int. J. Mol. Sci.* 22 (8) (2021) 4147, <https://doi.org/10.3390/ijms22084147>.
- [56] M. Cervantes, M. Cota, N. Arce, G. Castillo, E. Avelar, S. Espinoza, A. Morales, Effect of heat stress on performance and expression of selected amino acid and glucose transporters, HSP90, leptin and ghrelin in growing pigs, *J. Therm. Biol.* 59 (2016) 69–76, <https://doi.org/10.1016/j.jtherbio.2016.04.014>.
- [57] G. Pennarossa, S. Maffei, M.M. Rahman, G. Berruti, T.A.L. Brevini, F. Gandolfi, Characterization of the constitutive pig ovary heat shock chaperone machinery and its response to acute thermal stress or to seasonal variations, *Biol. Reprod.* 87 (5) (2012), <https://doi.org/10.1095/biolreprod.112.104018>.
- [58] J.T. Seibert, M.K. Adur, R.B. Schultz, P.Q. Thomas, Z.E. Kiefer, A.F. Keating, L.H. Baumgard, J.W. Ross, Differentiating between the effects of heat stress and lipopolysaccharide on the porcine ovarian heat shock protein response1, *J. Anim. Sci.* 97 (12) (2019) 4965–4973, <https://doi.org/10.1093/jas/skz343>.
- [59] N. Itami, K. Shirasuna, T. Kuwayama, H. Iwata, Short-term heat stress induces mitochondrial degradation and biogenesis and enhances mitochondrial quality in porcine oocytes, *J. Therm. Biol.* 74 (2018) 256–263, <https://doi.org/10.1016/j.jtherbio.2018.04.010>.
- [60] Y. Hao, Y. Feng, P. Yang, Y. Cui, J. Liu, C. Yang, X. Gu, Transcriptome analysis reveals that constant heat stress modifies the metabolism and structure of the porcine longissimus dorsi skeletal muscle, *Mol. Genet. Genom.* 291 (6) (2016) 2101–2115, <https://doi.org/10.1007/s00438-016-1242-8>.
- [61] Y. Hao, J.R. Liu, Y. Zhang, P.G. Yang, Y.J. Feng, Y.J. Cui, C.H. Yang, X.H. Gu, The microRNA expression profile in porcine skeletal muscle is changed by constant heat stress, *Anim. Genet.* 47 (3) (2016) 365–369, <https://doi.org/10.1111/age.12419>.
- [62] S.I.R. Montilla, T.P. Johnson, S.C. Pearce, D. Gardan-Salmon, N.K. Gabler, J.W. Ross, R.P. Rhoads, L.H. Baumgard, S.M. Lonergan, J.T. Selsby, Heat stress causes oxidative stress but not inflammatory signaling in porcine skeletal muscle, *Temperature* 1 (1) (2014) 42–50, <https://doi.org/10.4161/temp.28844>.

- [63] S. Ganesan, C. Reynolds, K. Hollinger, S.C. Pearce, N.K. Gabler, L.H. Baumgard, R.P. Rhoads, J.T. Selsby, Twelve hours of heat stress induces inflammatory signaling in porcine skeletal muscle, *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 310 (11) (2016) R1288–R1296, <https://doi.org/10.1152/ajpregu.00494.2015>.
- [64] S. Ganesan, O. Volodina, S.C. Pearce, N.K. Gabler, L.H. Baumgard, R.P. Rhoads, J.T. Selsby, Acute heat stress activated inflammatory signaling in porcine oxidative skeletal muscle, *Phys. Rep.* 5 (16) (2017), <https://doi.org/10.14814/phy2.13397>.
- [65] H. Zhang, B. Hu, J. Xiong, T. Chen, Q. Xi, J. Luo, Q. Jiang, J. Sun, Y. Zhang, Genomewide analysis of circular RNA in pituitaries of normal and heat-stressed sows, *BMC Genom.* 20 (1) (2019) 1013, <https://doi.org/10.1186/s12864-019-6377-7>.
- [66] P. Yang, Y. Hao, J. Feng, H. Lin, Y. Feng, X. Wu, X. Yang, X. Gu, The expression of carnosine and its effect on the antioxidant capacity of *Longissimus dorsi* muscle in finishing pigs exposed to constant heat stress, *Asian-Australas. J. Anim. Sci.* 27 (12) (2014) 1763–1772, <https://doi.org/10.5713/ajas.2014.14063>.
- [67] Y. Cui, Y. Hao, J. Li, Y. Gao, X. Gu, Proteomic changes of the porcine skeletal muscle in response to chronic heat stress, *J. Sci. Food Agric.* 98 (9) (2018) 3315–3323, <https://doi.org/10.1002/jsfa.8835>.
- [68] Y. Vashi, S. Naskar, T. Chutia, S. Banik, A.K. Singh, J. Goswami, V. Sejian, Comparative assessment of native, crossbred and exotic pigs during different seasons (winter, spring and summer) based on rhythmic changes in the levels of serum cortisol, lactate dehydrogenase levels and PBMC HSP70 mRNA expression pattern, *Biol. Rhythm. Res.* 49 (5) (2018) 725–734, <https://doi.org/10.1080/09291016.2017.1410019>.
- [69] T. Parkunan, D. Banerjee, N. Mohanty, P.K. Das, P. Ghosh, J. Mukherjee, A. Paul, A.K. Das, P.K. Nanda, S. Naskar, N.H. Mohan, M. Sarkar, B.C. Das, A comparative study on the expression profile of MCTs and HSPs in Ghungroo and Large White Yorkshire breeds of pigs during different seasons, *Cell Stress Chaperones* 20 (3) (2015) 441–449, <https://doi.org/10.1007/s12192-014-0569-5>.
- [70] [D.M. Voltolini, A.P. del Vesco, E. Gasparino, S.E.F. Guimarães, A.R. Oliveira Neto, E. Batista, A.P.S. Ton, Mitochondrial gene expression in the liver and muscle of high and low feed efficiency Japanese quail layers subjected to different environmental temperatures, *Genet. Mol. Res.* 13 (3) (2014) 4940–4948, <https://doi.org/10.4238/2014.July.4.8>.
- [71] S.H. Siddiqui, D. Kang, J. Park, H.W. Choi, K. Shim, Acute heat stress induces the differential expression of heat shock proteins in different sections of the small intestine of chickens based on exposure duration, *Animals* 10 (7) (2020) 1234, <https://doi.org/10.3390/ani10071234>.
- [72] R. Tóth, N. Tokodyné Szabadi, B. Lázár, K. Buda, B. Végi, J. Barna, E. Patakiné Várkonyi, K. Liptói, B. Pain, E. Gócza, Effect of post-hatch heat-treatment in heat-stressed Transylvanian naked neck chicken, *Animals* 11 (6) (2021) 1575, <https://doi.org/10.3390/ani11061575>.
- [73] J. Xie, L. Tang, L. Lu, L. Zhang, L. Xi, H.-C. Liu, J. Odle, X. Luo, Differential expression of heat shock transcription factors and heat shock proteins after acute and chronic heat stress in laying chickens (*Gallus gallus*), *PLoS One* 9 (7) (2014) e102204, <https://doi.org/10.1371/journal.pone.0102204>.
- [74] M.-B. Al-Zghoul, Z.B. Ismail, A.E.S. Dalab, A. Al-Ramadan, T.A. Althnaian, S.Y. Al-ramadan, A.M. Ali, I.F. Albokhadaim, K.A. al Busadah, A. Eljarah, K. I. Jawasreh, K.M. Hannon, Hsp90, Hsp60 and HSF-1 genes expression in muscle, heart and brain of thermally manipulated broiler chicken, *Res. Vet. Sci.* 99 (2015) 105–111, <https://doi.org/10.1016/j.rvsc.2014.12.014>.
- [75] J. Yang, J. Gu, Y. Hu, N. Wang, J. Gao, P. Wang, Molecular cloning and characterization of HSP60 gene in domestic pigeons (*Columba livia*) and differential expression patterns under temperature stress, *Cell Stress Chaperones* 26 (1) (2021) 115–127, <https://doi.org/10.1007/s12192-020-01160-7>.
- [76] K.R.B. Sporer, H.-R. Zhou, J.E. Linz, A.M. Booren, G.M. Strasburg, Differential expression of calcium-regulating genes in heat-stressed Turkey breast muscle is associated with meat quality, *Poultry Sci.* 91 (6) (2012) 1418–1424, <https://doi.org/10.3382/ps.2011-02039>.
- [77] Z. Lu, X. He, B. Ma, L. Zhang, J. Li, Y. Jiang, G. Zhou, F. Gao, Chronic heat stress impairs the quality of breast-muscle meat in broilers by affecting redox status and energy-substance metabolism, *J. Agric. Food Chem.* 65 (51) (2017) 11251–11258, <https://doi.org/10.1021/acs.jafc.7b04428>.
- [78] C.-Y. Cheng, W.-L. Tu, S.-H. Wang, P.-C. Tang, C.-F. Chen, H.-H. Chen, Y.-P. Lee, S.-E. Chen, S.-Y. Huang, Annotation of differential gene expression in small yellow follicles of a broiler-type strain of Taiwan country chickens in response to acute heat stress, *PLoS One* 10 (11) (2015) e0143418, <https://doi.org/10.1371/journal.pone.0143418>.
- [79] S.-H. Wang, C.-Y. Cheng, P.-C. Tang, C.-F. Chen, H.-H. Chen, Y.-P. Lee, S.-Y. Huang, Differential gene expressions in testes of L2 strain Taiwan country chicken in response to acute heat stress, *Theriogenology* 79 (2) (2013) 374–382.e7, <https://doi.org/10.1016/j.theriogenology.2012.10.010>.
- [80] E.M. Roushdy, A.W. Zagloul, M.S. El-Tarabany, Effects of chronic thermal stress on growth performance, carcass traits, antioxidant indices and the expression of HSP70, growth hormone and superoxide dismutase genes in two broiler strains, *J. Therm. Biol.* 74 (2018) 337–343, <https://doi.org/10.1016/j.jtherbio.2018.04.009>.
- [81] A.W. Zagloul, E.M. Roushdy, M.S. El-Tarabany, Impact of strain and duration of thermal stress on carcass yield, metabolic hormones, immunological indices and the expression of HSP90 and Myogenin genes in broilers, *Res. Vet. Sci.* 122 (2018) 193–199, <https://doi.org/10.1016/j.rvsc.2018.11.027>.
- [82] H. Cedraz, J.G.G. Gromboni, A.A.P. Garcia, R.V. Farias Filho, T.M. Souza, E. R. de Oliveira, E. B. de Oliveira, C. S. do Nascimento, C. Meneghetti, A. A. Wenceslau, Heat stress induces expression of HSP genes in genetically divergent chickens, *PLoS One* 12 (10) (2017) e0186083, <https://doi.org/10.1371/journal.pone.0186083>.
- [83] M.H. Tamzil, R.R. Noor, P.S. Hardjosworo, W. Manalu, C. Sumantri, Acute heat stress response of three lines of chicken with different heat stress protein (HSP) 70 genotype, *Int. J. Poultry Sci.* 12 (5) (2013) 264–272.
- [84] A. Galal, L.M. Radwan, H.H. Rezik, H. Ayoub, Expression levels of HSP70 and CPT-1 in three local breeds of chickens reared under normal or heat stress conditions after the introduction of the naked neck gene, *J. Therm. Biol.* 80 (2019) 113–118, <https://doi.org/10.1016/j.jtherbio.2018.12.018>.
- [85] A.L. Barreto Sánchez, Q. Wang, M. Thiam, Z. Wang, J. Zhang, Q. Zhang, N. Zhang, Q. Li, J. Wen, G. Zhao, Liver transcriptome response to heat stress in Beijing you chickens and Guang Ming broilers, *Genes* 13 (3) (2022) 416, <https://doi.org/10.3390/genes13030416>.